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Validity of nomograms relating the tensions of respiratory gases and pH in fetal blood*

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Estimation of the tensions of respiratory gases and pH in fetal blood has become more common in recent years since SALING [6] introduced sampling of fetal scalp blood during labor. Measurement of pH, pO_2 and pCO_2 in umbilical artery and vein blood is also used in the assessment of the condition of the newborn.

Because of the influence of pCO_2 on the O_2-content (BOHR effect), and of O_2-saturation, and consequently, of pO_2 on CO_2-content (HALDANE effect), there is an interdependence between pH, O_2-content, O_2-pressure, CO_2-content and CO_2-pressure. This relationship can be represented in the form of nomograms, enabling one to obtain the desired variables if at least two values are known.

EDWARDS et al. [1] established the first graphic representation of dissociation characteristics of respiratory gases in fetal blood. The nomogram constructed includes pO_2 and pCO_2 as well as O_2- and CO_2-contents. HELLEGERS et al. [3] provided a nomogram relating three variables in fetal blood: pO_2, pH and percent saturation of hemoglobin. FISCHER et al. [2] introduced the first nomogram depicting the interdependence of pO_2, O_2-content, percent saturation of hemoglobin, pCO_2, CO_2-content and pH, thus enabling one to derive four variables if the other two are known.

In order to examine the validity of these three nomograms, the six interdependent variables of pO_2, O_2-content, pH, pCO_2, CO_2-content and concentration of hemoglobin were measured directly in 25 samples of fetal blood. Measured values and those derived from the different nomograms were compared, and the percent deviation calculated. Each of the three nomograms delivered useful results, when it was used within physiological acid-base-balance.

* In memoriam ANDRE E. HELLEGERS.

Curriculum vitae

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1 Materials and methods

The blood of 25 newborn infants was used in this study. Fetal blood was obtained from the umbilical vein immediately after delivery. Blood was drawn into 10 ml syringes containing 0.2 ml of an oxalate-fluoride mixture consisting of 10% $K_2C_2O_4$ and 5% NaF [5].

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Blood samples were equilibrated in 2 ml tonometers [4] containing various mixtures of oxygen and carbon dioxide. Oxygen tensions were used which were likely to produce hemoglobin saturations varying between 20 and 80%. The carbon dioxide tensions used were chosen to provide wide variations in the ultimate pH and the oxygen saturation of the blood sample. Equilibration was allowed in a water bath at 38 °C for 30 minutes. After equilibration, blood samples were drawn anaerobically into oiled syringes and analyzed.

Equilibrated gas mixtures were analyzed by the method of SCHOLANDER [7]. Blood was analyzed for oxygen and carbon dioxide content by the micromanometric method of VAN SLYKE et al. [9]; the pO_2 and pCO_2 were measured by means of an IL-blood gas analyzer. Percent saturation of hemoglobin was calculated from the hemoglobin concentration determined photometrically, because means for direct measurement were not available. The pH of each equilibrated blood sample was estimated by the micro-pH-method of SIGGAARD-ANDERSEN et al. [8]. A total of 150 equilibrations were performed and 900 values were determined.

The different nomograms were examined on the basis that pH, pO_2 and pCO_2 are the most commonly measured values. Thus the nomogram of EDWARDS et al. [1] was entered with pO_2 and pCO_2. The O_2-content and CO_2-content were obtained from the nomogram and compared with the measured values of the blood samples. HELLEGERS et al. nomogram [3] was entered with the mandatory factors of pH and pO_2. Percent hemoglobin saturation was read and compared with the calculated value. The nomogram of FISCHER et al. [2] was used twice: First, pH and pO_2 were entered and the percent saturation was read; second, the nomogram was entered with pO_2 and pCO_2, and the variables of O_2- and CO_2-content were derived. For each parameter taken into consideration, the absolute and percentage differences between obtained and measured values were determined. Mean and standard deviation of the percentage differences were calculated. Thus 1782 values of the three nomograms were verified. The results of the nomograms of EDWARDS et al. [1] and HELLEGERS et al. [3] were compared with those of the nomogram of FISCHER et al. [2] using the corresponding variables for entry.

2 Results

Fig. 1 presents the d'Ocagne nomogram for fetal whole blood constructed by EDWARDS et al. [1]. O_2- and CO_2-contents were read by entering the nomogram with pO_2 and pCO_2. The number of cases (N), mean ($\bar{x}$) and standard deviation (s) of percent differences between observed and calculated values are listed in Tabs. Ia and Ib. Using two oxygen partial pressures (15 mmHg and 40 mmHg), O_2-contents derived from that nomogram were too low in the case of high pCO_2 (80 mmHg) and too high in the case of low pCO_2 (20 mmHg). CO_2-contents are not to be read at high CO_2-tensions; there is always a positive

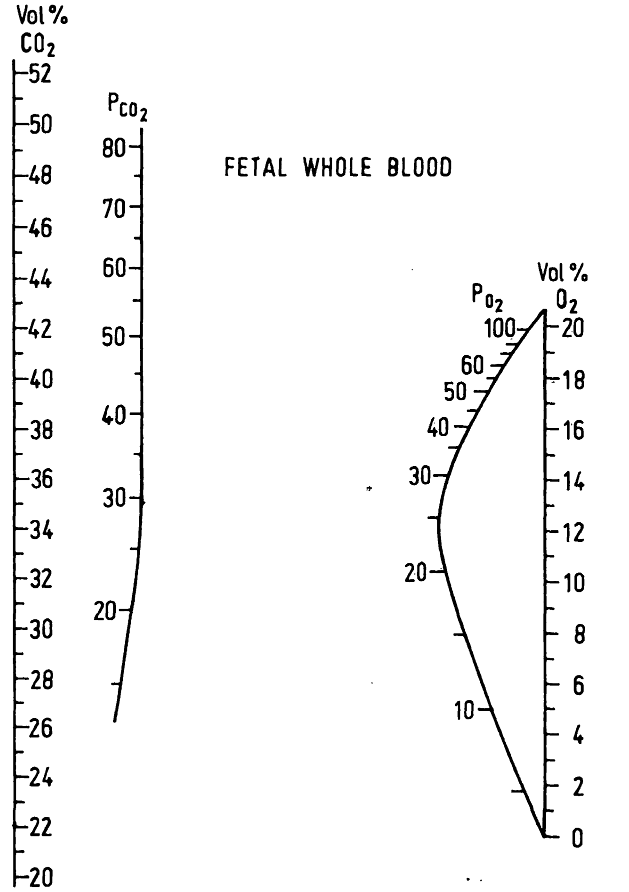

Fig. 1. Fetal blood gas dissociation curves on the d'Ocagne nomogram according to EDWARDS et al. [1].
Vol% CO_2 = CO_2-content (Vol%); pCO_2 = CO_2-tension (mmHg); pO_2 = O_2-tension (mmHg); Vol% O_2 = O_2-content (Vol%)

Tab. Ia. %Differences between observed and calculated values of O_2-content (EDWARD and ROSS nomogram).

Equilibration pO_2 (mmHg)	pCO_2 (mmHg)	N	%Difference between observed and calculated O_2-content ($\bar{x} \pm s$)
15	80	25	- 18.9 ± 20.3
15	40	25	6.9 ± 25.4
15	20	25	24.3 ± 30.5
		total 75	4.1 ± 31.0
40	80	25	- 4.6 ± 12.2
40	40	25	- 1.1 ± 11.8
40	20	25	2.6 ± 10.5
		total 75	- 1.0 ± 11.8

Tab. Ib. %Differences between observed and calculated values of CO_2-content (EDWARD and ROSS nomogram).

Equilibration pO_2 (mmHg)	pCO_2 (mmHg)	N	%Difference between observed and calculated CO_2-content ($\bar{x} \pm s$)
15	80	–	–
15	40	25	11.7 ± 20.6
15	20	25	37.7 ± 55.1
		total 50	24.7 ± 43.2
40	80	–	–
40	40	25	8.7 ± 21.7
40	20	25	35.0 ± 42.5
		total 50	21.9 ± 36.0

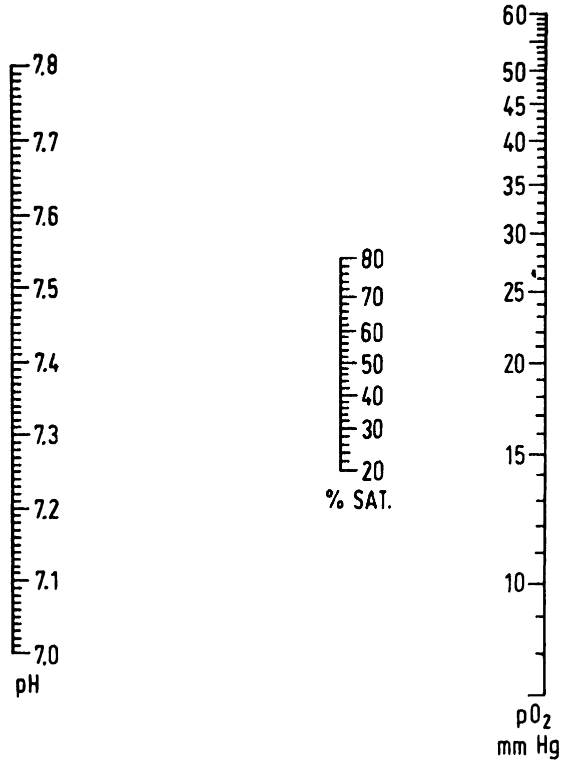

Fig. 2. Nomogram for oxygen dissociation curve of fetal blood according to HELLEGERS et al. [3].
%SAT. = percent hemoglobin saturation; pO_2 = O_2-tension (mmHg)

deviation in CO_2-content regardless of the absolute values of pO_2 and pCO_2.

Fig. 2 demonstrates the nomogram for the O_2-dissociation curve of fetal blood published by HELLEGERS et al. [3]. The percent saturation of hemoglobin was obtained from the nomogram using pH and pO_2 for entry. Tab. II shows the mean ($\bar{x}$) and standard deviation (s) of the percentage differences between observed and calculated hemoglobin saturation. The derived saturation values were consistently lower than the measured values, independent of given pO_2 and pCO_2.

Fig. 3 represents the respiratory gas and acid base nomogram established by FISCHER et al. [2]. The relationship of six interdependent variables to eachother is plotted in a CARTESIAN nomogram. In order to compare the results, the nomogram was entered in two different fashions. Using pO_2 and pCO_2 for entry, O_2- and CO_2-content were obtained as in EDWARDS et al. [1] nomogram (Tabs. IIIa and IIIb). Percent saturation of hemoglobin was ascertained by entering the nomogram with pH and pO_2 as in the HELLEGERS et al. [3] nomogram, and the results are presented in Tab. IIIc. The derived O_2-contents were always higher than the measured ones, the error being less at a higher pO_2. The calculated data of CO_2-content were too high at low pCO_2 and vice versa. The calculated saturation of hemoglobin was found to be too low with decreasing pCO_2.

Tab. II. %Differences between observed and calculated values of hemoglobin saturation (HELLEGERS and SCHRUEFER nomogram).

Equilibration pO2 (mmHg)	pCO2 (mmHg)	N	%Difference between observed and calculated hemoglobin saturation ($\bar{x} \pm s$)
15	80	3	- 10.8 ± 1.0
15	40	17	- 9.0 ± 10.0
15	20	23	- 8.4 ± 12.1
		total 43	- 8.8 ± 10.7
40	80	24	- 10.5 ± 9.5
40	40	23	- 10.3 ± 6.5
40	20	15	- 10.9 ± 6.4
		total 62	- 10.5 ± 7.6

Tab. IIIa. %Differences between observed and calculated values of O_2-content (FISHER, VOGEL and THEWS nomogram).

Equilibration pO2 (mmHg)	pCO2 (mmHg)	N	%Difference between observed and calculated O2-content ($\bar{x} \pm s$)
15	80	25	15.5 ± 26.2
15	40	25	12.9 ± 25.3
15	20	25	12.3 ± 25.9
		total 75	13.5 ± 25.5
40	80	25	3.0 ± 12.8
40	40	25	4.6 ± 10.8
40	20	25	4.7 ± 10.8
		total 75	4.1 ± 11.4

Tab. IIIb. %Differences between observed and calculated values of CO_2-content (FISHER, VOGEL and THEWS nomogram).

Equilibration pO2 (mmHg)	pCO2 (mmHg)	N	%Difference between observed and calculated CO2-content ($\bar{x} \pm s$)
15	80	–	–
15	40	25	- 8.9 ± 22.3
15	20	25	12.2 ± 44.8
		total 50	1.7 ± 36.5
40	80	25	- 20.1 ± 8.7
40	40	25	- 8.5 ± 18.1
40	20	25	15.3 ± 36.0
		total 75	- 4.4 ± 27.8

Tab. IIIc. %Differences between observed and calculated values of hemoglobin saturation (FISHER, VOGEL and THEWS nomogram).

Equilibration pO2 (mmHg)	pCO2 (mmHg)	N	%Difference between observed and calculated hemoglobin saturation ($\bar{x} \pm s$)
15	80	21	15.8 ± 17.6
15	40	20	0.2 ± 18.9
15	20	14	- 1.7 ± 17.4
		total 55	5.7 ± 19.4
40	80	17	- 2.6 ± 7.3
40	40	25	- 6.0 ± 6.2
40	20	21	- 6.8 ± 5.6
		total 63	- 5.3 ± 6.5

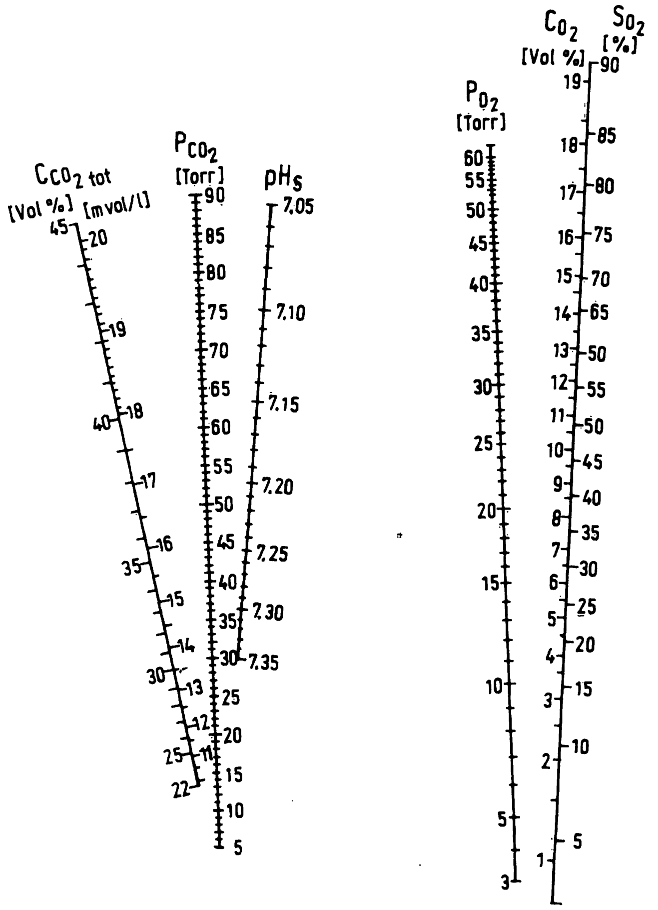

Fig. 3. Nomogram for respiratory gas and acid base status of fetal blood according to FISCHER et al. [2].
C CO_2 tot = CO_2-content (Vol% and meq/L); pCO_2 = CO_2-tension (mmHg); pH_S = pH value of plasma; pO_2 = O_2-tension (mmHg); C O_2 = O_2-content (Vol%); S O_2 = percentage saturation of hemoglobin

3 Discussion

Investigation of EDWARDS et al. [1] nomogram showed that the mean percentage deviation between obtained and measured O_2-contents (Tab. Ia) was 4.1 ± 31,0% when pO_2 = 15 mmHg, and - 1.0 ± 11.8% when pO_2 = 40 mmHg. In the range of pCO_2 = 80 mmHg, the deviation was negative, i. e. the obtained O_2-concentrations were too low. CO_2-content is not to be read from the nomogram if pCO_2 is above 80 mmHg. In the case of normal pCO_2 (40 mmHg) and low pCO_2 (20 mmHg), the mean percentage deviation from measured CO_2-content was virtually independent of pO_2 (Tab. Ib). Entry with low CO_2-tensions lead to a mean percentage deviation of more than one third. EDWARDS et al. [1] nomogram therefore delivers O_2- and CO_2-contents within a mean deviation close to 10% if pO_2 ranges between 15 and 40 mmHg, and pCO_2 is approximately 40 mmHg.

For FISCHER et al. [2] nomogram, at a low pO_2 the mean percent deviation between observed and calculated oxygen content was almost independent of pCO_2 (13.5 ± 25.5%; Tab. IIIa). The same phenomenon was observed when pO_2 levels were moderate, at 40 mmHg (4.1 ± 11.4%). Thus, O_2-contents obtained from the nomogram of FISCHER et al. have a more constant and pCO_2-independent deviation of about 8%. CO_2-content cannot be read in this nomogram if pO_2 = 15 mmHg and pCO_2 = 80 mmHg. In the remaining pO_2-pCO_2-combinations, this nomogram yielded CO_2-contents that were too low in the case of high CO_2-tensions, and vice versa (Tab. IIIb). Comparing CO_2-contents obtained from the nomogram of EDWARDS et al. (Tab. Ib) and those from the FISCHER et al. nomogram (Tab. IIIb), the latter had a smaller deviation if physiological O_2- and CO_2-tensions of fetal blood were used. At "nonphysiological" low pCO_2 (20 mmHg), the mean percent deviation of calculated CO_2-content was remarkably lower according to FISCHER et al. nomogram.

Entering the nomogram of HELLEGERS et al. [3] with pH and pO_2, the percent saturation of hemoglobin was obtained. The overall mean percentage deviation was approximately - 10%, independent of pO_2 and pCO_2 (Tab. II). When the same variables were entered into the FISCHER et al. nomogram, the percent deviation of calculated saturation was 5.7 ± 19.4% in the case of low pO_2, and - 5.3 ± 6.5% if pO_2 was 40 mmHg (Tab. IIIc). With increasing pCO_2 values the percent deviation increased with low, and decreased with high O_2-tensions, so that the error in calculated saturation became larger with the combination of a low pO_2 and a high pCO_2, and vice versa. This seems to be due to the inaccuracy of the nomogram at either extreme. It is probably for this reason that HELLEGERS et al. nomogram ranges only from 20 to 80% saturation. Furthermore, one must consider that the absolute difference between measured and derived values leads to a larger or smaller percent deviation, depending on the magnitude of the original values.

A final evaluation of the three investigated nomograms stems from the fact that, for the use of any nomogram, pH and pO_2 or pO_2 and pCO_2 must be known, variables which are commonly measured in fetal blood analyses. HELLEGERS et al. nomogram requires pH and pO_2. The obtained percent saturation of hemoglobin is consistently about 10% too low. EDWARDS et al. nomogram requires the determination of pO_2 and pCO_2 for entry. Respiratory gas contents can be derived with varying errors depending on the given gas tensions. For the use of the nomogram published by FISCHER et al. pO_2 and pCO_2 or pH are required, thus offering two possibilities for entry. The theoretical possibility of entering the nomogram with pH and pCO_2 must be discarded since it yields incalculable failures in the derived parameters because of the close relationship of pH and pCO_2, as shown in the HENDERSON-HASSELBALCH equation. Using either pO_2 and pH, or pO_2 and pCO_2 for entry respiratory gas contents as well as percent saturation of hemoglobin can be obtained from the FISCHER et al. nomogram. Derived O_2-contents are for the most part too high, especially at low pO_2 values; CO_2-contents are too high at low pCO_2 and vice versa. The percent deviation differs mainly at extreme combinations of O_2- and CO_2-pressures.

Within the physiological range any nomogram can be used with tolerable deflections. The nomogram of FISCHER et al. however, seems to be handier because of the versatile entry and the greater number of obtainable variables.

Summary

Respiratory gas tensions and pH in fetal blood can be obtained from nomograms constructed by EDWARDS et al. [1], HELLEGERS et al. [3] and FISCHER et al. [2] on the basis of the interdependence of pO_2, O_2-content, percentage saturation of hemoglobin, pCO_2, CO_2-content and pH. If two variables are known the desired ones can be derived from the nomogram.

In order to verify the published nomograms, 25 fetal blood samples were equilibrated with six different oxygen and carbon dioxide gas mixtures, analysed by the method of SCHOLANDER [7]. Oxygen and carbon dioxide contents were determined by micromanometric method of VAN SLYKE et al. [9]. Actual pH was estimated by the micromethod of SIGGAARD-ANDERSEN et al. [8]. Percentage saturation was calculated from the hemoglobin concentration measured photometrically.

The nomograms under investigation were entered with the required parameters and desired variables were read. Absolute and percentage differences between measured and obtained values were estimated and mean as well as standard deviation of the percentage difference were calculated.

O_2-contents derived from the nomogram of EDWARDS et al. [1] are too low in case of a high pCO_2 and vice versa; CO_2-contents obtained from that nomogram have a tolerable deviation only at the normal range of arterial carbon dioxide tension.

Percentage saturation of hemoglobin derived from the nomogram of HELLEGERS et al. [3] is about ten percent too low independent of actual pO_2 and pCO_2.

The nomogram of FISCHER et al. [2] allows to obtain O_2- and CO_2-contents as well as percentage saturation of hemoglobin. O_2-contents read from this nomogram are in good accordance with the estimated values at increasing pO_2 and vice versa; percentage saturation of hemoglobin deviates tolerably, especially within the physiogical range of saturation.

Each of the studied nomograms seems to be reliable within certain limits. The nomogram of FISCHER et al. however, provided additional advantages.

Keywords: Acid-base-calculation, fetal blood, pH, respiratory gases, whole blood nomograms.

Zusammenfassung

Die Gültigkeit von Nomogrammen zur Bestimmung von pH und Atemgasdrucken im fetalen Blut

Nomogramme zur Bestimmung von Atemgasgrößen und Säure-Basen-Werten aus dem fetalen Blut wurden von EDWARDS et al. [1], HELLEGERS et al. [3] und FISCHER et al. [2] angegeben. Sie alle beruhen auf der gegenseitigen Abhängigkeit von pO_2, Sauerstoffgehalt, prozentualer Sauerstoffsättigung, pCO_2, Kohlendioxidgehalt und pH. Sind zwei der Variablen bekannt, können die fehlenden nomographisch bestimmt werden.

Um die Genauigkeit der angegebenen Nomogramme zu überprüfen wurden 25 fetale Blutproben mit sechs verschiedenen Sauerstoff-Kohlendioxid-Gemischen equilibriert. Ihre Zusammensetzung wurde nach der Methode von SCHOLANDER [7] bestimmt. Der Sauerstoff- und Kohlendioxidgehalt im Blut wurden mikromanometrisch nach VAN SLYKE et al. [9] gemessen. Die von SIGAARD-ANDERSEN et al. [8] angegebene Mikromethode diente zur Messung des aktuellen pH, während der Berechnung der Sauerstoffsättigung die photometrisch bestimmte Hämoglobinkonzentration zu Grunde lag.

Die dabei erhaltenen Parameter wurden benutzt, um in die einzelnen Nomogramme einzugehen. Aus den prozentualen Differenzen, die zwischen gemessenem und nomographisch ermitteltem Wert entstanden, wurden dann Mittelwert und Standardabweichung berechnet.

Generell läßt sich sagen, daß der Sauerstoffgehalt, wenn er aus dem Nomogramm von EDWARDS et al. [1] ermittelt wurde, bei hohem Kohlendioxidpartialdruck zu niedrig und bei niedrigem zu hoch ausfiel; während der Kohlendioxidgehalt tolerable Abweichungen nur bei einem pCO_2 von etwa 40 mmHg aufwies.

Wurde die Sauerstoffsättigung aus dem Nomogramm von HELLEGERS et al. [3] ermittelt, waren die Werte stets etwa zehn Prozent zu hoch; eine Abhängigkeit von Sauerstoff- und Kohlendioxidpartialdruck ließ sich dabei nicht erkennen. Das Nomogramm von FISCHER et al. [2] bietet bei bekanntem pH, pO_2 und pCO_2 die Möglichkeit, einerseits den Sauerstoff- und Kohlendioxidgehalt und andererseits die Sauerstoffsättigung zu ermitteln. Sauerstoffgehalte, die aus diesem Nomogramm bestimmt wurden, korrelierten um so mehr mit den gemessenen Werten, je höher der aktuelle Sauerstoffpartialdruck war und umgekehrt; die Sauerstoffsättigung wich im physiologischen Bereich in annehmbaren Grenzen ab.

Jedes der betrachteten Nomogramme lieferte brauchbare Ergebnisse, da die groben Abweichungen nur bei extremen Partialdrucken auftraten. Das Nomogramm von FISCHER et al. bietet allerdings mehr Variationsmöglichkeiten.

Schlüsselwörter: Atemgase, fetales Blut, Nomogramme für Vollblut, pH, Säure-Basen-Bestimmung.

Résumé

La validité des nomogrammes concernant la tension des gaz respiratoires et le pH du sang fœtal

On peut obtenir la tension du gaz respiratoires et le pH du sang fœtal par des nomogrammes d'EDWARDS et al. [1], d'HELLEGERS et al. [3] et de FISCHER et al. [2]. Les nomogrammes basent sur l'interdépendance de la tension et de la concentration de l'oxygène, de la saturation d'hémoglobine, de la tension et de la concentration d'acide carbonique et du pH. Si on a deux de ces paramètres on peut lire la valeur demandée dans le nomogramme.

Pour vérifier ces nomogrammes, 25 analyses du sang fœtal étaient équilibrées avec six mélanges differentes d'oxygène et d'acide carbonique analysées par la méthode de SCHOLANDER [7]. Les concentrationes d'oxygène et d'acide carbonique étaient déterminées par le micromanomètre de VAN SLYKE et al. [9]. Le pH actuel était détermié par la méthode de SIGGAARD-ANDERSEN et al. [8]. La saturation était calculée de la concentration d'hémoglobine, qui était déterminée par un photomètre.

On inscrirait dans les nomogrammes à vérification les valeurs mesurées et obtenait les valeurs désirées. Les différences absolues et le pourcentage entre les valeurs mesurées obtenues étaient recherchées et le moyen et la déviation standardisée était calculée.

La concentration d'oxygène obtenue du nomogramme d'EDWARDS et al. [1] étaient trop bas en cas de tension d'oxygène haute et vice versa; la concentration d'acide carbonique obtenue de ce nomogramme a une déviation tolérable mais seulement en cas de tension d'acide carbonique normale.

La saturation d'hémoglobine en pourcentage derivé du nomogramme d'HELLEGERS et al. [3] est à peu près dix pourcent trop bas indépendent de la tension d'oxygène et la tension d'acide carbonique.

Le nomogramme de FISCHER et al. [2] permet d'obtenir la concentration d'oxygène et d'acide carbonique et aussi la saturation pourcentage d'hémoglobine. Les concentrations d'oxygène lues du nomogramme correspondent bien aux valeurs mesurées sous des tensions d'oxygène montantes. Les concentrations recherchées d'acide carbonique sont trop hautes en cas de tension d'acide carbonique bas et vice versa. La saturation pourcentage d'hémoglobine dévit tolérablement, particulièrement dans la la sphère physiologique.

Tous de ces nomogrammes contrôlés semblent être sûr en limites fixées, le nomogramme de FISCHER et al. donne des avantages supplémentaires.

Mots-clés: Détermination de la relation, gaz respiratoires, nomogrammes du sang fœtal, pH, relation acide-base, sang fœtal.

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